Is schizophrenia a neurodevelopmental disorder?

SIR,—In response to our leading article (19 September, p 681) Drs John L Waddington and Hanafy A Youssef point out (17 October, p 997) that schizophrenic patients with tardive dyskinesia have an excess of "developmental (primitive/neonatal) reflexes" and suggest that schizophrenics with anomalies in brain development are particularly susceptible to tardive dyskinesia. Their idea is an interesting one which is supported by the evidence that some preschizophrenics may already show involuntary movements[1] and also by the finding of Bartels and others[2] that tardive dyskinesia is especially common in "non-genetic schizophrenia"; we have shown that a history of pregnancy and birth complications is obtained more frequently from schizophrenics without a family history of psychiatric disorder than from those with such a history.[3]

Drs S J Cooper and D J King (24 October, p 1068) take us to task for regarding the possible aetiological roles of viral infections and birth complications as separate. We did not make our views clear enough; certainly we accept that viral infections during pregnancy may induce growth or other abnormalities in the fetus leading to secondary perinatal complications. The importance of viral infection during pregnancy has recently been emphasised by Mednick *et al*, who studied the rates of schizophrenia in young adults exposed during fetal life to the influenza epidemic which swept Helsinki in 1957[4]; those exposed to the epidemic during their second trimester of fetal development had an increased risk of later schizophrenia.

Dr M T Abou-Saleh (14 November, p 1278) suggests that brain damage caused by obstetric complications explains the scan abnormalities and cognitive deficits commonly found in so called type II schizophrenia. We concur with this and suggest that the deficits of affect and cognition which are seen in this type of chronic schizophrenia are actually continuations of longstanding deficits present before the onset of psychosis and dating from the initial brain insult. This goes against the traditional notion of schizophrenia as a deteriorating disorder.[5] Dr Abou-Saleh's point about higher rates of perinatal injury in developing countries is not easily resolved. We would simply note that severe mental retardation is a syndrome which numbers obstetric injury among its causes; yet, like schizophrenia, it shows a surprisingly stable global incidence.

Dr Abou-Saleh also states that it is difficult to reconcile the neurodevelopmental hypothesis with the genetic basis of the disorder but then goes on to suggest that early developmental anomaly might involve the very brain structures which mediate the effects of genetic factors. Exactly! Mednick *et al* consider that "a part of the genetic vulnerability to schizophrenia consists of a heightened sensitivity of the brain to perinatal insult."[4] Considerable evidence implicates the hippocampus. The genetic predisposition to schizophrenia might well comprise the inheritance of a pattern of neuronal migration into the hippocampus which is especially vulnerable to hypoxic-ischaemic damage.[5]

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1 Manschreck TC. Motor abnormalities in schizophrenic patients. In: Nasrallah HA, Weinberger DR. *The neurology of schizophrenia*. Amsterdam: Elsevier, 1986.
2 Bartels M, Mann K, Friedrich W. Tardive dyskinesia: marked predominance of nongenetic schizophrenia. *Biol Psychiatry* 1985;20:94-119.
3 Lewis SW, Murray RM. Obstetric complications, neuro-developmental deviance and risk of schizophrenia. *J Psychiatr Res* (in press).
4 Mednick SA, Parnas J, Schulsinger F. The Copenhagen high-risk project, 1962-86. *Schizophr Bull* 1987;13:485-95.
5 Murray RM, Lewis SW, Owen MJ, Foerster A. The neurodevelopmental origins of dementia praecox. In: McGuffin P, Bebbington P, eds. *Schizophrenia: the major issues*. London: William Heinemann (in press).

The Royal College of Psychiatrists and South Africa

SIR,—Dr Alistair King (5 December, p 1488) asks how the Royal College of Psychiatrists "gives in so easily to a group of bigoted and narrow minded anti-South Africa extremists."

The damage which apartheid policies have caused to South Africa's people in terms of both health and health services in general and psychiatric services in particular has been well and repeatedly documented. The appalling contrasts in living conditions between whites and blacks are described, for instance, in the report of the Commonwealth Eminent Persons Group,[1] which contains such "bigoted extremists" as Malcolm Fraser, Lord Barber, and the Primate of the Anglican Church of Canada. Their visit was part of the Commonwealth's response to the problems raised by South Africa, which led to the Commonwealth's Nassau Accord. This made a number of recommendations, which included "a discouragement of all cultural and scientific events except where these contribute towards the ending of apartheid or have no possible role in promoting it." This was adopted as a policy by our college earlier this year.

Its interpretation is, of course, a matter of debate, and we have specifically excluded the possibility of a complete academic boycott of South Africa. The original purpose of Professor Simpson's visit, and the reason for his invitation, was for him to give an account of his experience to a committee of our college which is particularly concerned with the abuse of psychiatry. This purpose was achieved.

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1 Commonwealth Eminent Persons Group. *Mission to South Africa*. (Commonwealth report, 1986.) London: Penguin Books, 1986.

Advanced training for ambulance crews

SIR,—In the article by Dr J M Rowley and colleagues (28 November, p 1387) the number of lives saved when ambulancemen used basic resuscitation techniques and defibrillation only was impressive.

In Chester we operate a flying squad service manned by a doctor which responds at the request of the first ambulance crew or general practitioner to attend collapsed patients. Our experience of out of hospital cardiac arrests is rather different. In the past 30 months 90 patients with cardiac arrest have been attended, 11 of whom have ultimately survived to leave hospital (12%). All the survivors were in ventricular fibrillation, but in only two cases were cardiac rhythms re-established using defibrillation alone. The remaining survivors required intubation and the administration of intravenous drugs as well as defibrillation before a pulse was re-established.

I would commend the use of defibrillators by emergency medical or paramedical staff who are first to attend collapsed patients. Our experience implies that back up by staff trained in the more advanced techniques of resuscitation would save even more lives. I would therefore support both supplying all ambulances with defibrillators and the development of a second tier service manned by staff with advanced training.

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SIR,—It seems that Dr J M Rowley and others (28 November, p 1387) have failed to imagine the aspects of this subject that lie outside the confines of their own discipline.

I wholeheartedly agree with their conclusion that the new training for ambulancemen is "an example of the excellent being the enemy of the good" if only the treatment of cardiac arrest is considered. In that situation, yes, the primary need is to defibrillate—and quickly.

Ambulances have this funny habit, however, of being called to patients who have been injured in car accidents and have suffered blood loss or have lost control of their airway or to patients who have taken too much insulin and need 50% dextrose fast—to name but two simple examples. In these life threatening but reversible conditions the timely intervention of an ambulanceman who can put up an infusion of plasma expander, support the airway, and if necessary intubate or give the required intravenous energy quickly may make the difference between the patient's next port of call being the hospital or the mortuary.

Of course, good cardiac care is an important skill for ambulancemen. So, too, is good trauma care and good life support care generally. Please, gentlemen, off with the blinkers.

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Toxic myocarditis in paracetamol poisoning

SIR,—We agree that there is evidence for toxic myocarditis in some cases of fulminant hepatic failure, including those due to paracetamol poisoning (31 October, p 1097), but many of the features described by Dr Riadh A Wakeel and others are consistent with a diagnosis of uncontrolled cerebral oedema and, ultimately, brain stem compression rather than features of cardiotoxicity per se.[1,2]

The sinus tachycardia followed by sudden arrhythmia, hypotension, altered level of consciousness, dilated pupils, absent brain stem reflexes, respiratory depression, and cardiac asystole are all consistent with such changes.[1,2] That absent pupillary responses and brain stem reflexes can be reversed in some cases by hyperventilation and by a mannitol induced diuresis would strongly suggest that uncontrolled cerebral oedema is at least a factor in their cause.[3] The absence of visible tonsillar compression at necropsy does not, in our experience, exclude brain stem coning as a mode of death, and the authors noted the presence of diffuse cerebral oedema. This is particularly important since early recognition and intensive control of cerebral oedema is a major factor in achieving a survival of 50-60% from fulminant hepatic failure even in those who reach grade III-IV encephalopathy.[3,4] We would have considered this 15 year old patient to have had a relatively good prognosis despite the undoubted severity of the poisoning in view of her youth, the maintained urine output, low level of serum creatinine, and maximum prothrombin time of only 65 seconds.

The pathological findings of Dr Wakeel and

others would certainly point to a myocardial element, although we would also question whether left ventricular dilatation and pulmonary oedema might, in addition to acute cardiac failure, reflect fluid overload.[5] The pulmonary wedge pressures were not stated.

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1 Weston MJ, Talbot IC, Howorth PJN, *et al.* Frequency of arrhythmias and other cardiac abnormalities in fulminant hepatic failure. *Br Heart J* 1976;38:1179-88.
2 Trewby PN, Williams R. Pathophysiology of hypotension in patients with fulminant hepatic failure. *Gut* 1977;18:1021-6.
3 Ede R, Williams R. Hepatic encephalopathy and cerebral edema. *Semin Liver Dis* 1986;6:107-18.
4 O'Grady JG, Gimson AES, O'Brien CJ, *et al.* Controlled trials of charcoal hemoperfusion and prognostic factors in fulminant hepatic failure. *Gastroenterology* (in press).
5 Bihari DJ, Gimson AES, Williams R. Cardiovascular, pulmonary and renal complications of fulminant hepatic failure. *Semin Liver Dis* 1986;6:119-28.

AUTHORS' REPLY,—Dr Fagan and her colleagues agree with the basic issue that toxic myocarditis is seen in some cases of paracetamol poisoning. They also acknowledge that left ventricular dilatation and pulmonary oedema seen at necropsy reflect acute cardiac failure. We would like to assure them that our patient received the standard treatment for cerebral oedema, including intravenous mannitol and hyperventilation, but without success. Fluid intake exceeded output by less than 1 litre in 21 hours, and, allowing for invisible water loss and a mild degree of dehydration, the total fluid intake was appropriate. Fluid overload was therefore unlikely.

It is true that some of the features they refer to can be attributed to uncontrolled cerebral oedema, but cerebral oedema can itself be a consequence of hypoxia complicating arrhythmia and hypotension. Furthermore, they use the term "brain stem coning" rather loosely and suggest that the mere presence of cerebral odema without tonsillar compression is equivalent to brain stem coning. This statement is a departure from accepted teaching in pathology. It raises another important question relating to the grade of cerebral oedema which they consider equivalent to brain stem coning. Such a flexible interpretation lacks precision and must therefore be rejected.

Nevertheless, some deaths from paracetamol poisoning occur without evidence of hepatic necrosis at necropsy. In a study cited by Meredith *et al* 61 out of 65 patients who died outside hospital showed no hepatic necrosis at necropsy.[1] Such an alarmingly high figure should not be attributed to factors like the concomitant intake of drugs or alcohol without considering other possibilities including that of paracetamol induced arrhythmia.[2] In a report on the failure of naloxone to reverse the cardiotoxic effect of dextropropoxyphene, a component of Distalgesic, the authors recorded bizarre complexes of hypotension.[3] Their patient later arrested and was successfully resuscitated. Unfortunately, they failed to recognise that paracetamol might have been the cause. An interesting feature which this patient shared with ours was the poor clearance of paracetamol from the plasma. We believe there is enough evidence in the case we reported to suggest myocardial toxicity from paracetamol.

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1 Meredith TJ, Prescott LF, Vale JA. Why do patients still die from paracetamol poisoning? *Br Med J* 1986;293:345-6.
2 Will EJ, Tomkins AM. Acute myocardial necrosis in paracetamol poisoning. *Br Med J* 1971;iv:430-1.
3 Barraclough CJ, Lowe RA. Failure of naloxone to reverse the cardiotoxicity of Distalgesic overdose. *Postgrad Med J* 1982;58:667-8.

Charging patients for eye tests

SIR,—While there is much in the government's white paper *Promoting Better Health* which could improve the provision of primary health care there are potentially serious implications in the introduction of charges to patients for eye tests.

Diabetes mellitus is the leading cause of blindness in people of working age in the United Kingdom.[1] Treatment with photocoagulation of both proliferative retinopathy and maculopathy can prevent some 60% of blindness,[2 3] but the changes must be detected early. Regular funduscopy is performed on patients attending diabetic clinics, but less than half of all known diabetic patients attend clinics, the remainder obtaining all supplies from their general practitioners.[4-6] These patients are much less likely to have regular funduscopy.[4] Moreover, on a general practitioner's list of 2000 patients there will be 20 diabetics, so that even if that general practitioner performs annual dilated funduscopy on all non-clinic attenders this will comprise only 10 examinations a year. As the prevalence of retinopathy is around 30% and of sight threatening retinopathy 10%[7] the general practitioner will be extremely unlikely to obtain the experience necessary to provide an effective role in screening.

Two studies have shown that optometrists detect serious retinopathy with high sensitivity.[8 9] These results and the anxiety expressed by general practitioners about their ability to detect retinopathy have encouraged many to work with local optometrists in providing comprehensive screening for their diabetic patients.

In this district we are piloting a study, funded by the British Diabetic Association, to evaluate the benefits of a computerised register of diabetic patients.[10] The computer will be used to prompt general practitioners and patients about regular examinations and blood tests. Because of the anxieties of the participating general practitioners over funduscopy we have agreed with local optometrists that they will screen for retinopathy by funduscopy after the instillation of mydriatic drops.

In a district with a population of 200 000 half of the 2000 known diabetics would not be attending a hospital. The incidence of sight threatening retinopathy is 1·2% a year,[7] which corresponds to 12 cases a year in these non-hospital attenders, and photocoagulation could prevent blindness in seven of these patients. Using Foulds's figure of £3500 as the annual cost to the state of supporting a blind person[7] it is possible to perform a simple cost-benefit analysis of retinal screening by optometrists under the present system of reimbursing £9.30 for the eye test: costs of screening 1000 diabetic patients—£9300; benefits of preventing seven cases of blindness—£24 500.

At a time when an effective treatment has been introduced for treating retinopathy and when the DHSS itself is looking at ways of screening effectively for diabetic retinopathy,[11] no major hurdle should be introduced to the screening role of the optometrist. The introduction of an exemption category so that diabetic patients would continue to obtain free eye tests would help to answer this problem, but other difficulties would remain. Some 8% of diabetic patients have retinopathy at diagnosis,[12] and changes in refraction produced by high blood glucose concentrations are responsible for many patients with undiagnosed diabetes attending an optometrist. The fact that optometrists are often responsible for diagnosis in these patients means that they have an important role in screening for disease as well as detecting complications. It is therefore important that the free eye test should remain.

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1 Sorsby A. *The incidence and causes of blindness in England and Wales 1963-1968.* London: HMSO, 1972. (DHSS Reports on Public Health and Medical Subjects No 128.)
2 British Multicentre Study Group. Photocoagulation for diabetic maculopathy. A randomised controlled study using the xenon-arc. *Diabetes* 1983;32:1010-6.
3 British Multicentre Study Group. Photocoagulation for proliferative diabetic retinopathy: a randomised controlled trial using the xenon-arc laser. *Diabetologia* 1984;26:109-15.
4 Yudkin JS, Boucher BJ, Schopflin KE, *et al.* The quality of diabetic care in a London health district. *J Epidemiol Community Health* 1980;34:277-80.
5 Fleming PC. What is happening to our diabetic patients? An audit of care in general practice. *Practical Diabetes* 1985;2:26-9.
6 Doney BJ. An audit of care of diabetics in group practice. *J R Coll Gen Pract* 1976;26:734-42.
7 Foulds WS, McCuish A, Barrie T, *et al.* Diabetic retinopathy in the west of Scotland: its detection and prevalence and the cost-effectiveness of a proposed screening programme. *Health Bull (Edin)* 1983;41:318-26.
8 Burns-Cox CJ, Dean Hart JC. Screening of diabetics for retinopathy by ophthalmic opticians. *Br Med J* 1985;290:1052-4.
9 Hill RD. Screening for diabetic retinopathy at primary care level. *Diabetologia* 1981;20:670.
10 Hurwitz BS, Solomonides AE, Wilsher D, Yudkin JS. A diabetic data base and prompting system to improve community care. *Diabetic Medicine* 1987;4:357.
11 Bron AJ. Screening for treatable diabetic retinopathy. *Br Med J* 1985;290:1025-6.
12 Herron CA. Screening in diabetes mellitus: report of the Atlanta workshop. *Diabetes Care* 1979;2:357-62.

Graduated compression and its relation to venous refilling time

SIR,—The disbelief of Professor A N Nicolaides and his colleagues at St Mary's Hospital (5 December, p 1484), that our "careful studies" (31 October, p 1087) did not agree with their own long term clinical experience requires objective evidence.

We are entirely satisfied that the techniques we used were reproducible, and all the investigations were performed by a single person. There would appear to be a basic scientific flaw in the argument they have put forward, since whatever failing they may claim in the use of photoplethysmography, this flaw must then be equally distributed among all the studies, and, as the technician concerned had no preconceived knowledge of the possible results and was thus effectively blinded, we do not see how these factors could have biased the results.

We have, however, considerably more data than those published in this paper and have confirmed the work by using photoplethysmography with no defect being necessary in the garment, and also with a small group of patients studied by volume refilling using a strain gauge plethysmograph. Our results have been confirmed by the group working at St George's Hospital, who also extended their data to include use of venous pressures.[1] It is most unfortunate that the extensive studies quoted from St Mary's do not seem to have been published.

We appreciate the potential limitations of our classification and can confirm that all patients included within the deep venous incompetence group had phlebographic evidence of incompetence at popliteal level. One might, however, speculate on the need to attempt a pure separation in the face of equivalent defects in venous function.

The clear statistical significance of the results, albeit in small numbers of patients, to us would confirm the clinical importance of these results.